Center for Neuroscience and Regenerative Medicine

USU Discussion Group

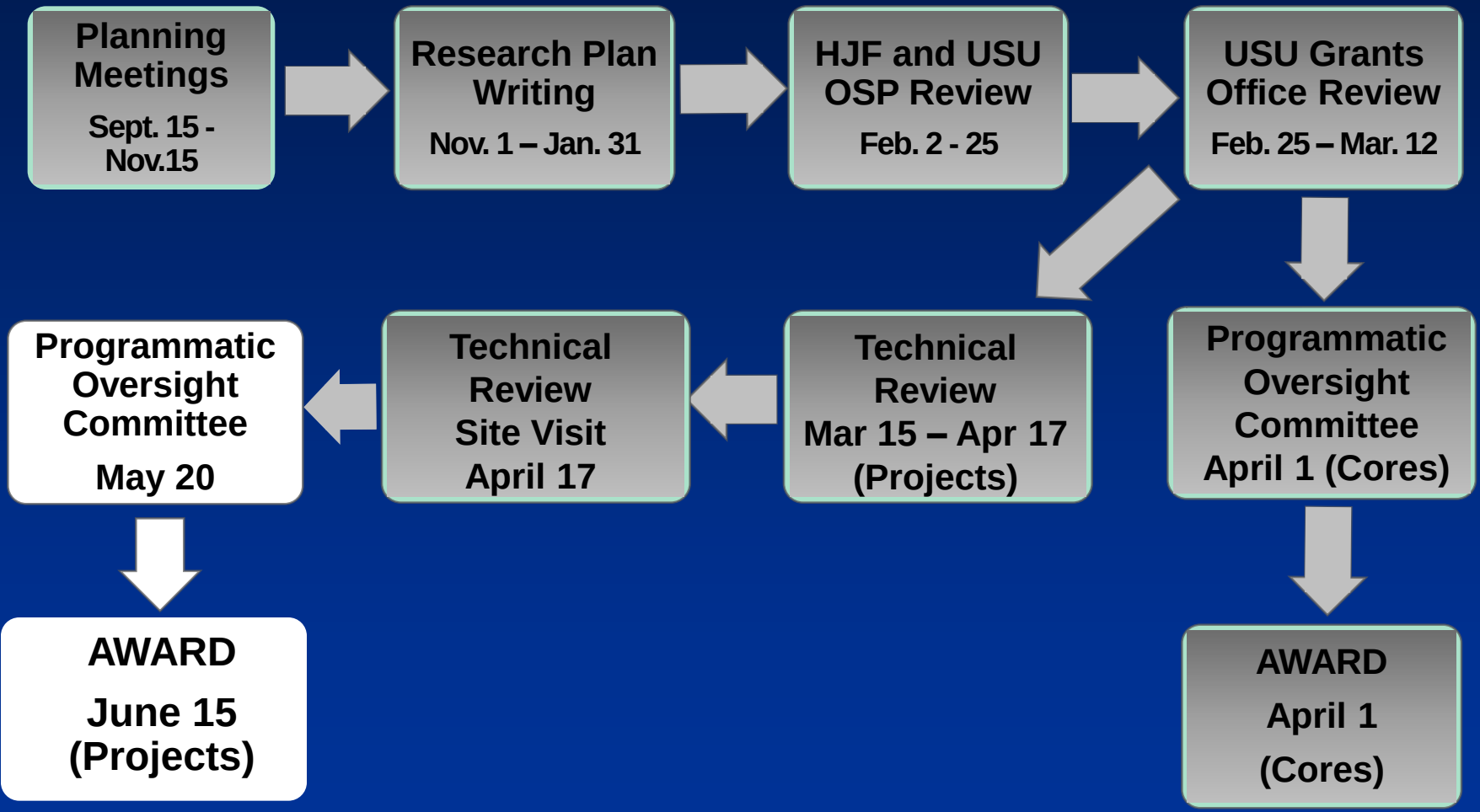
August 20, 2009

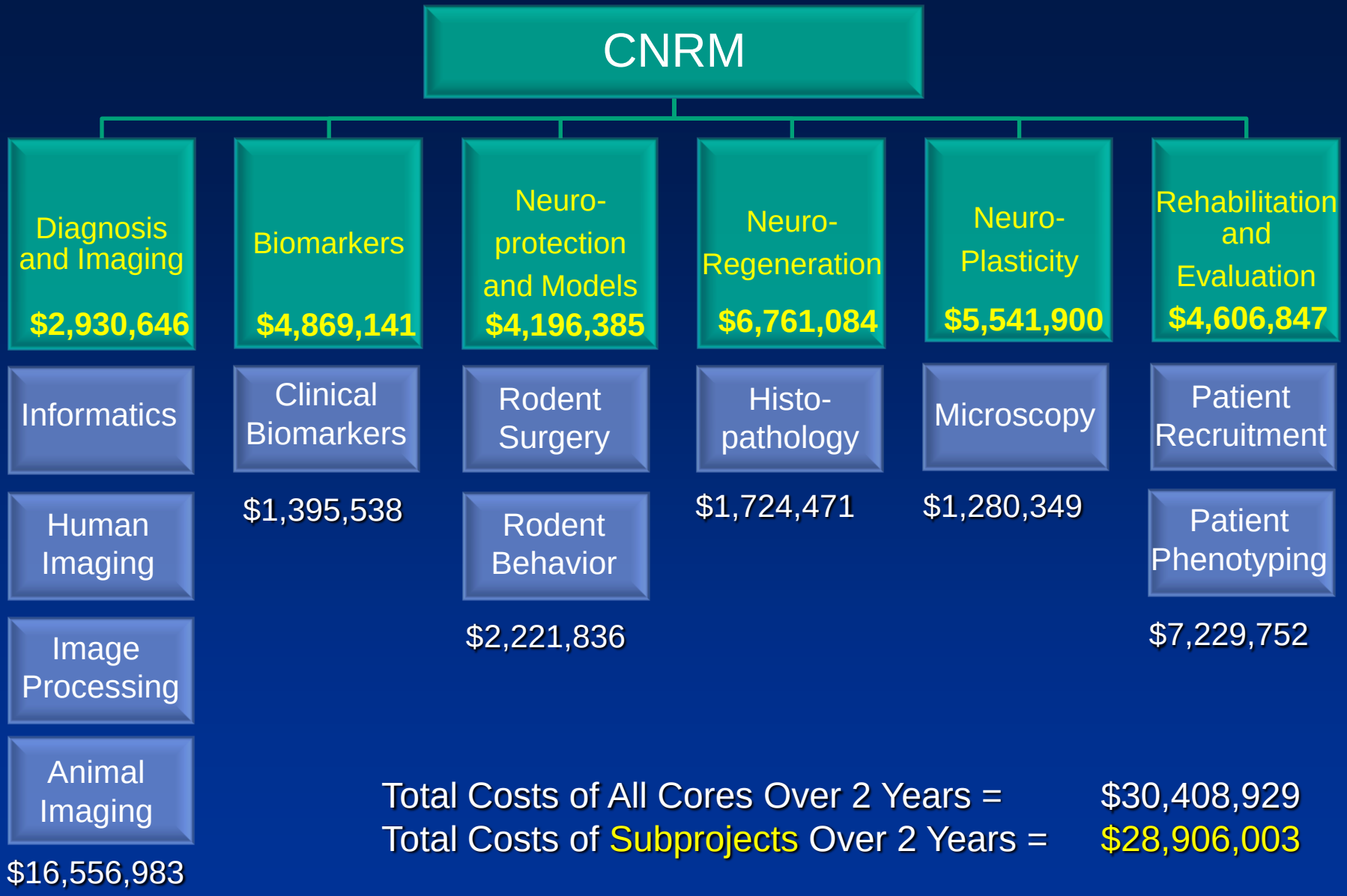
CNRM
CENTER FOR NEUROSCIENCE AND REGENERATIVE MEDICINE

A Catalyst For Brain Injury Research

NATIONAL INSTITUTES OF HEALTH

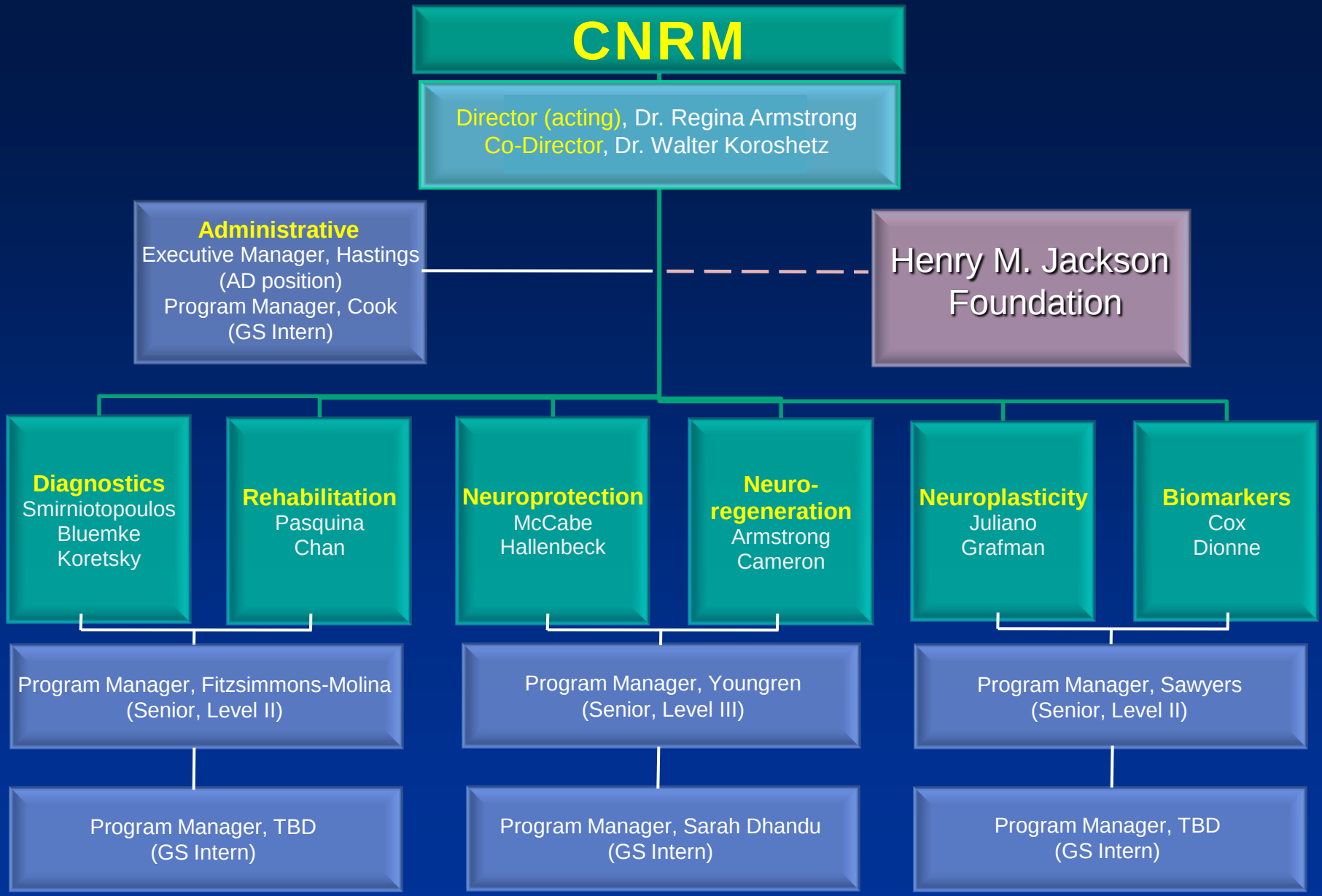
CNRM Program Review Process





Total Costs of All Cores Over 2 Years = $30,408,929

Total Costs of Subprojects Over 2 Years = $28,906,003


CNRM
Director (acting), Dr. Regina Armstrong
Co-Director, Dr. Walter Koroshetz
Administrative
Executive Manager, Hastings
(AD position)
Program Manager, Cook
(GS Intern)
Henry M. Jackson Foundation
Diagnostics
Smirniotopoulos
Bluemke
Koretsky
Rehabilitation
Pasquina
Chan
Neuroprotection
McCabe
Hallenbeck
Neuro-regeneration
Armstrong
Cameron
Neuroplasticity
Juliano
Grafman
Biomarkers
Cox
Dionne
Program Manager, Fitzsimmons-Molina
(Senior, Level II)
Program Manager, Youngren
(Senior, Level III)
Program Manager, Sawyers
(Senior, Level II)
Program Manager, TBD
(GS Intern)
Program Manager, Sarah Dhandu
(GS Intern)
Program Manager, TBD
(GS Intern)

CNRM Leased Space

12725 Twinbrook Parkway in Rockville, MD

Occupancy in early September, 2009

Patient Recruitment Core Plan

- **PI:** Raymond Dionne, DDS, Ph.D., NINR/NIH
- **Coordinated system = single face of CNRM to each study subject**
- Minimize the burden on TBI subjects
- Maximize inclusion into protocols
- Integrate clinical information with follow-up into elected plans for biomarkers, phenotyping, and imaging studies
- Use study personnel effectively

Clinical Biomarkers Core Plan

- **PI:** Raymond Dionne, DDS, Ph.D., NINR/NIH
- **Biosamples**
  - Prospectively collected blood, cerebrospinal fluid (CSF), and surgically removed brain tissues (as appropriate)
  - TBI patients and non - TBI controls
  - Standardized procedures for research across CNRM
  - Include collection of clinical and demographic data
  - Biorepository to include human and animal specimens
- **Coordinated with Recruitment Core**

Informatics Core Plan

- **PI:** Yang Fann, Ph.D., NINDS/NIH (acting)
- Integrated system to serve all CNRM activities:

Investigators :

1) web-based data entry and data management system for all human subjects, to anonymize and integrate the demographic, phenotypic, neuroimaging, and available biomarkers. System to provide regular reports on overall enrollment, eligibility of subjects for various projects, IRB protocol tracking. Intent is to build compatible DOD-common data element program and DOD-CIT federal TBI/PH database.

2) web-based entry of CNRM pre-clinical research results.

Administrative Core: project milestones, budgets, personnel, publications, reporting needs, etc.

Human Studies Committee: coordination of protocol plans, patient involvement, outcomes monitoring, etc.

Human Imaging Core Plan

- **PI:** Jim Smirniotopoulos, M.D., USU
- **Co-PI:** David Bluemke, M.D., Ph.D, CC/NIH
- **Goal: Provide infrastructure for current and future advanced neuroimaging of CNRM patients.**
- **Functions (NIH/CC):**

- **Develop human, whole body 3T PET/MRI** scanner as platform for CNRM advanced neuroimaging, with manufacturer

Years 1 - 2:

- PET/CT for metabolic and biochemical imaging (novel ligands)
- Replace both units with integrated PET /MRI by end of initial 2 years

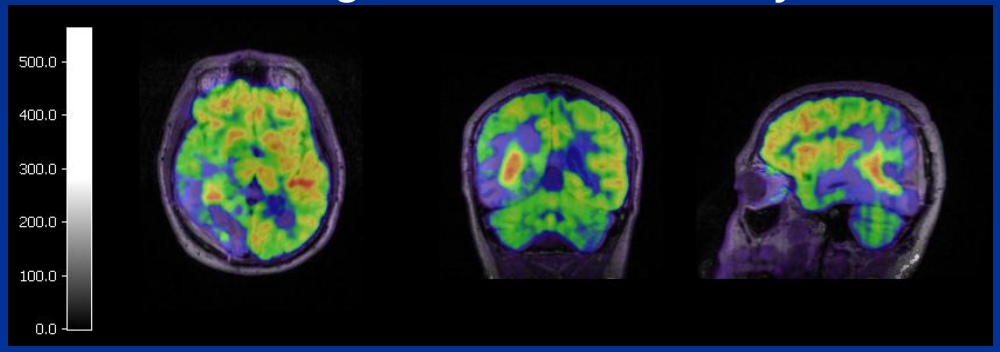
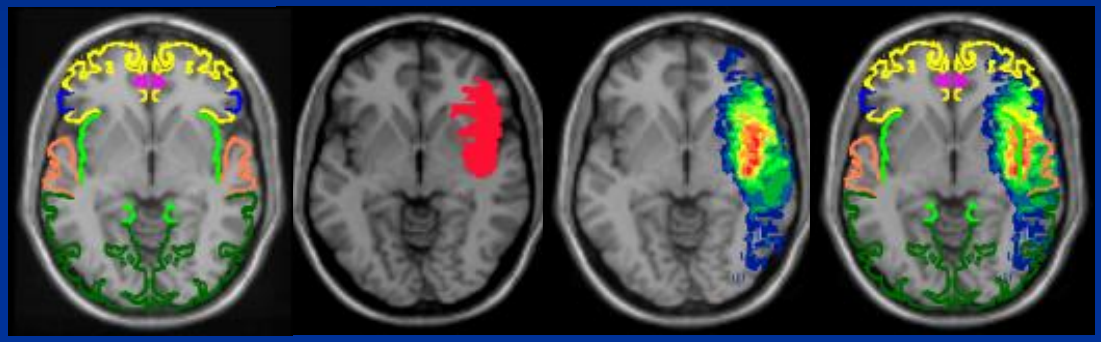


Image Processing Core Plan

- **PI:** John Butman, M.D., Ph.D., CC/NIH
- **Coordinated system to transform raw imaging data into usable forms that can then be accessed by all members of the CNRM.**
- **Functions:**

- Data repository with quality control and format control
- Automated image pre-processing, registration, and segmentation
- Quantitation mapping (physiologic, functional, structural)
- Lesion analysis (manual and automated segmentation)
- Accessibility of processed data



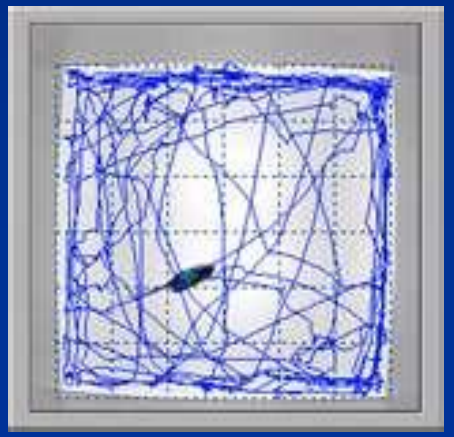
Animal Imaging Core Plan

- **PI:** Reed Selwyn, Ph.D., USU Radiology
- **MRI 9.4T imaging of TBI models**
- **Major Functions**

- *In vivo* structural and functional MR analysis to correlate with histopathology
- Integration of structural and functional MR data with behavioral and neurological assessments, especially in longitudinal studies
- Monitoring of stem cell localization and migration

Behavior Core Plan

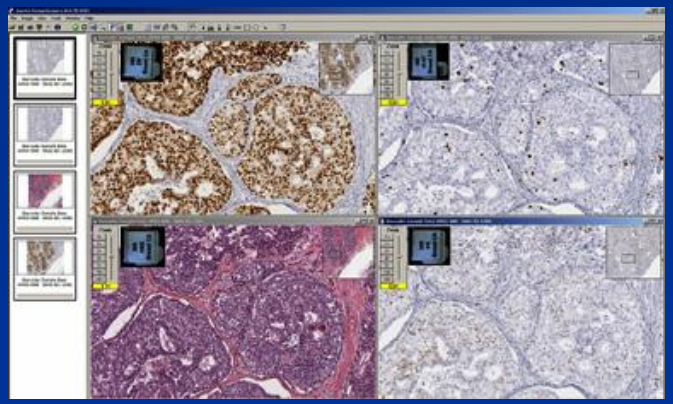
- **PI:** Joe McCabe, Ph.D., USU
- Provide facilities and training for highest standards of behavioral assessment across CNRM projects for longitudinal tracking of functional changes in models of TBI.
- Neurological functions (including olfaction and corpus callosum), motor coordination, nociception, learning and memory, anxiety, cognition, social interaction
- Mouse behavior as new core set up and
- Rat behavior as collaborative studies with Dr. Neil Grunberg



Histopathology Core Plan

- **PI:** Regina Armstrong, Ph.D., USU
- **Process and digitize human and animal tissue sections for neuropathological analysis**

- Human tissues through AFIP to assist characterization of TBI
- Rodent tissues, especially as needed for animal models of TBI
- Digitizing to facilitate access, analysis, and entry into database
- Equipment for automated staining of tissue sections
- Coordinate tissue sectioning with *in vivo* and *ex vivo* MRI



Microscopy Core Plan

- **PI:** Sharon Juliano, Ph.D., USU
- **Correlation of structural and functional features in tissues using high resolution microscopy with electrophysiology.**
  - Two photon fluorescence microscopy
  - Electron microscopy
  - Optical imaging
  - Quantitative analysis of images using stereology
  - Reside within USU BIC
- **Personnel:**

  Technician (100%)

  Instructor (50%)

Patient Phenotyping Core Plan

- **PI:** Leighton Chan, M.D., CC/NIH
- **Coordinated Phenotyping System**

- Assessments of the entire spectrum of patients in CNRM studies
- Integrate with Biomarkers and Human Imaging Cores
- Characterize patients who display evidence of overlap symptoms related to both TBI and PTSD.
- Collect data prospectively and retrospectively to match TBI common data elements, including: demographics, re-injury and injury-related data, neurologic examination, symptoms, treatment, neuroimaging

Phenotyping

- **“TBI” is poorly defined**
- **Spectrum disorder with cluster of anatomic and physiologic findings, symptom complexes, and variable outcomes.**
- **Access to health records:**
  - 400 Penetrating trauma
  - 850 Amputees
  - 1600 WRAMC patients
- **More sophisticated measurement tools**
  - Validated outcome measures
  - Neurocom/CAREN
  - Neuroimaging

Faculty Recruitment Plan

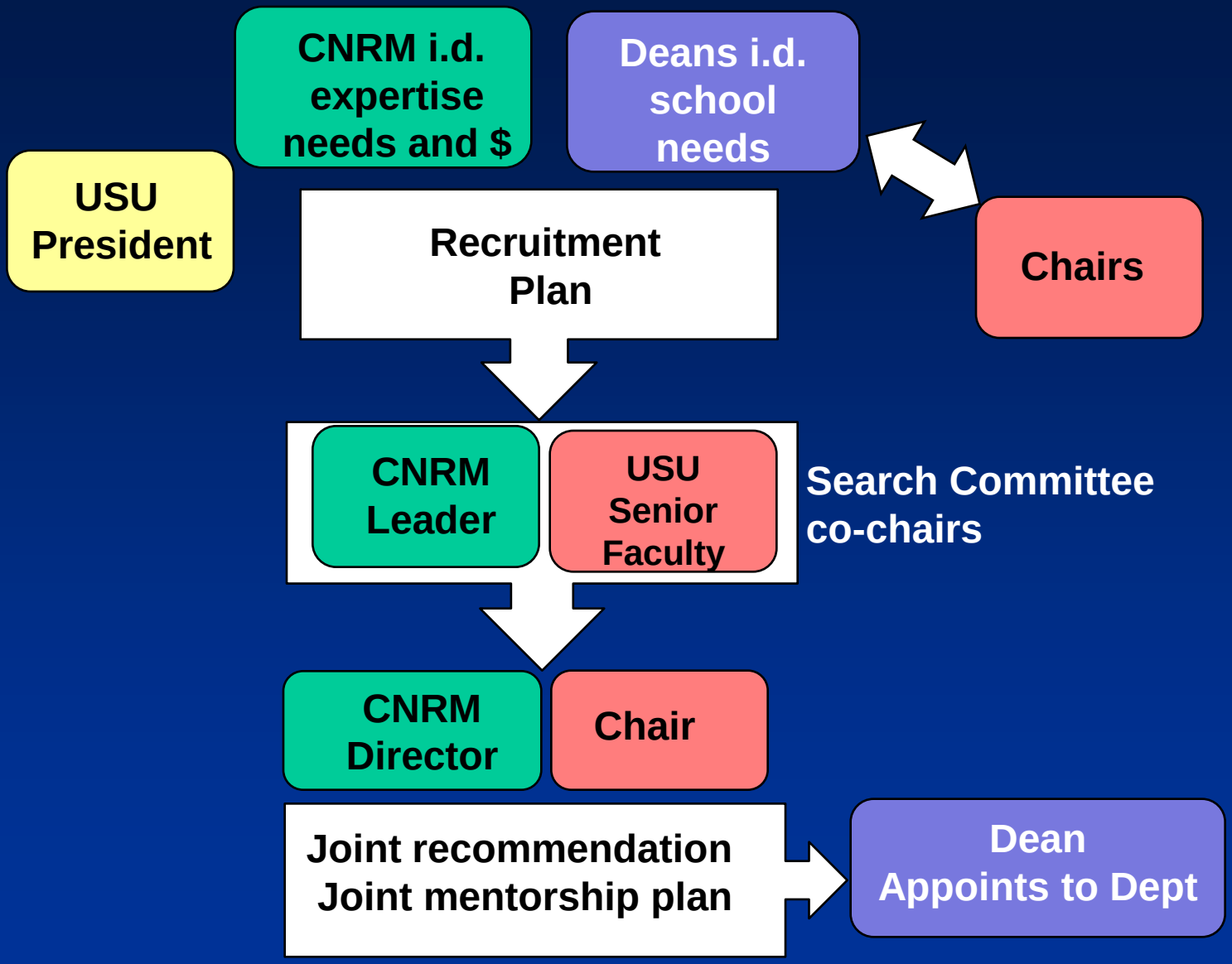
Initial Set:

1. Clinician (M.D.) with (acute) head injury expertise and ability to lead a strong, collaborative clinical research program. SOM, Neurology Department.

2. Neuropathologist (M.D.) to lead research program that can interface with AFIP, NIH, and USU investigators. SOM, Pathology Department.

3. Nurse researcher (Ph.D.) with head injury expertise and ability to lead a strong, collaborative research program. GSN.

CNRM Governance for Faculty Recruitment



NIH interactions…

NATIONAL INSTITUTES OF HEALTH

Future Communications

- CNRM Website (www.usuhs.mil/cnrm/)

- USU Discussion Group meetings scheduled approximately quarterly. Tentative dates:

  November 19, 2009 at 4:00

  February 18, 2010 at 4:00

  May 20, 2010 at 4:00